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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: IMMUNE RESPONSE ASSOCIATED PROTEINS

(57) Abstract: ABSTRACT OF THE DISCLOSURE Various embodiments of the invention provide human immune response associated proteins (IRAP) and polynucleotides which identify and encode IRAP. Embodiments of the invention also provide expression vectors, host cells, antibodies, agonists, and antagonists. Other embodiments provide methods for diagnosing, treating, or preventing disorders associated with aberrant expression of IRAP.

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INTERNATIONAL SEARCH REPORT

Inte[redacted]hal application No.
PCT/US03/26988

Box I Observations where certain claims were found unsearchable (C ntinuation of Item 1 of first sheet)

This international report has not been established in respect f certain claims under Article 17(2)(a) for the f llowing reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claim Nos.: 21,22,24 and 25
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
Please See Continuation Sheet

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1, 2, 17, 18, and 56 as drawn to SEQ ID NO: 1

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application N .

PCT/US03/26988

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07K 14/47

US CL : 530/350; 435/69.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 530/350; 435/69.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ARUFFO, A. et al. The lymphocyte glycoprotein CD6 contains a repeated domain structure characteristic of a new family of cell surface and secreted proteins. J. Exp. Med. October 1991, Vol. 174, No. 4, pages 949-952. The CD6 isoform is 86.7% identical to SEQ ID NO: 1 and 99.1% identical over residues 17-122 of SEQ ID NO: 1.	1 and 17
X	BOWEN, M.A. et al., Structure and chromosomal location of the human CD6 gene: detection of five human CD6 isoforms. J. Immunol. February 1997, Vol. 158, No. 3, page 1149-1156. The CD6 isoform is 86.7% identical to SEQ ID NO: 1 and 99.1% identical over residues 17-122 of SEQ ID NO: 1.	1 and 17

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"B" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

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Form PCT/ISA/210 (second sheet) (July 1998)

C ntinuation of Box I Reason 2:
Claims 21, 22, 24, and 25 are unsearchable because the description and claims are so unclear that no meaningful search could be performed. Claim 21 is drawn to a composition identified by the method of claim 20. The composition has yet to be identified. Claim 22 is drawn to a method for treating a disease by administering the unidentified composition of claim 21. Claim 24 is drawn to an antagonist compound identified by the method of claim 23, which has yet to be identified. Claim 25 is drawn to a method for treating a disease by administering the unidentified antagonist of claim 24. Because the compositions are not defined in the specification, it would be impossible to search both the compositions and methods of using the compositions.

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1, claims 1, 2, 17, 18, and 56, in part, drawn to isolated polypeptides comprising SEQ ID NO: 1 and variants and immunogenic fragments thereof. If Group 1 is elected, the claims will be searched to the extent that they read on SEQ ID NO: 1.

Groups 2-35, claims 1, 2, 17, 18, and 57-90, in part, drawn to isolated polypeptides comprising SEQ ID NOS: 2-35 and variants and immunogenic fragments thereof, respectively. If Group 2 is elected, the claims will be searched to the extent that they read on SEQ ID NO 2. If Group 3 is elected, the claims will be searched to the extent that they read on SEQ ID NO: 3. If Group 4 is elected, the claims will be searched to the extent that they read on SEQ ID NO: 4, and so on. If Applicant elects one of Groups 2-35130, please indicate which SEQ ID NO is to be searched.

Groups 36-70, claims 3-7, 9, 10, 12, 13, 48-55, and 91-125, in part, drawn to isolated polynucleotides comprising SEQ ID NOS: 36-70, respectively, recombinant polynucleotides, host cells, methods of expressing DNA, methods of culturing host cells, and arrays. If Group 36 is elected, the claims will be searched to the extent that they read on SEQ ID NO: 36. If Group 37 is elected, the claims will be searched to the extent that they read on SEQ ID NO: 37. If Group 38 is elected, the claims will be searched to the extent that they read on SEQ ID NO: 38. If Group 39 is elected, the claims will be searched to the extent that they read on SEQ ID NO: 39, and so on. If Applicant elects one of Groups 36-70, please indicate which SEQ ID NO is to be searched.

Groups 71-105, claim 8, in part, drawn to transgenic organisms comprising recombinant polynucleotides comprising SEQ ID NOS: 36-70, respectively. If Group 71 is elected, the claims will be searched to the extent that they read on a transgenic organism comprising a recombinant polynucleotide comprising SEQ ID NO: 36. If Group 72 is elected, the claims will be searched to the extent that they read on a transgenic organism comprising a recombinant polynucleotide comprising SEQ ID NO: 37. If Group 73 is elected, the claims will be searched to the extent that they read on a transgenic organism comprising a recombinant polynucleotide comprising SEQ ID NO: 38. If Group 74 is elected, the claims will be searched to the extent that they read on a transgenic organism comprising a recombinant polynucleotide comprising SEQ ID NO: 39, and so on. If Applicant elects one of Groups 71-105, please indicate which SEQ ID NO is to be searched.

Groups 106-140, claims 11, 31-32, 34, 37-38, and 40-43, in part, drawn to antibodies that bind to polypeptides comprising SEQ ID NOS: 1-35, respectively. If Group 106 is elected, the claims will be searched to the extent that they read on an antibody that binds to a polypeptide comprising SEQ ID NO: 1. If Group 107 is elected, the claims will be searched to the extent that they read on an antibody that binds to a polypeptide comprising SEQ ID NO: 2. If Group 108 is elected, the claims will be searched to the extent that they read on an antibody that binds to a polypeptide comprising SEQ ID NO: 3. If Group 109 is elected, the claims will be searched to the extent that they read on an antibody that binds to a polypeptide comprising SEQ ID NO: 4, and so on. If Applicant elects one of Groups 106-140, please indicate which SEQ ID NO is to be searched.

Groups 141-175, claims 14-16, in part, drawn to methods of detecting target polynucleotides comprising SEQ ID NOS: 36-70, respectively. If Group 141 is elected, the claims will be searched to the extent that they read on a method of detecting a polynucleotide comprising SEQ ID NO: 36. If Group 142 is elected, the claims will be searched to the extent that they read on a method of detecting a polynucleotide comprising SEQ ID NO: 37. If Group 143 is elected, the claims will be searched to the extent that they read on a method of detecting a polynucleotide comprising SEQ ID NO: 38. If Group 144 is elected, the claims will be

searched to the extent that they read on a method of detecting a polynucleotide comprising SEQ ID NO: 39, and so on. If Applicant elects one of Groups 141-175, please indicate which SEQ ID NO is to be searched.

Groups 176-210, claim 19, in part, drawn t methods for treating disease by administering polypeptides comprising SEQ ID NOS: 1-35, respectively. If Group 176 is elected, the claim will be searched to the extent that they read on a method of treating a disease by administering a polypeptide comprising SEQ ID NO: 1. If Group 177 is elected, the claim will be searched to the extent that they read on a method of treating a disease by administering a polypeptide comprising SEQ ID NO: 2. If Group 178 is elected, the claim will be searched to the extent that they read on a method of treating a disease by administering a polypeptide comprising SEQ ID NO: 3. If Group 179 is elected, the claim will be searched to the extent that they read on a method of treating a disease by administering a polypeptide comprising SEQ ID NO: 4, and so on. If Applicant elects one of Groups 176-210, please indicate which SEQ ID NO is t be searched.

Groups 211-245, claims 20, 23, 26, and 27, in part, drawn to a method of screening for compounds that modulate the activity of polypeptides comprising SEQ ID NOS: 1-25, respectively. If Group 126 is elected, the claims will be searched to the extent that they read on a method of screening for compounds that modulate the activity of a polypeptide comprising SEQ ID NO: 1. If Group 127 is elected, the claims will be searched to the extent that they read on a method of screening for compounds that modulate the activity of a polypeptide comprising SEQ ID NO: 2. If Group 128 is elected, the claims will be searched to the extent that they read on a method of screening for compounds that modulate the activity of a polypeptide comprising SEQ ID NO: 3. If Group 129 is elected, the claims will be searched to the extent that they read on a method of screening for compounds that modulate the activity of a polypeptide comprising SEQ ID NO: 4, and so on. If Applicant elects one of Groups 126-150, please indicate which SEQ ID NO is to be searched.

Groups 246-280, claim 28, in part, drawn to a method of screening a compound for effectiveness in altering the expression of a polynucleotide comprising SEQ ID NO: 36-70, respectively. If Group 246 is elected, the claim will be searched to the extent that it reads on a method of screening a compound for effectiveness in altering the expression of a polynucleotide comprising SEQ ID NO: 36. If Group 247 is elected, the claim will be searched to the extent that it reads on a method of screening a compound for effectiveness in altering the expression of a polynucleotide comprising SEQ ID NO: 37. If Group 248 is elected, the claim will be searched to the extent that it reads on a method of screening a compound for effectiveness in altering the expression of a polynucleotide comprising SEQ ID NO: 38. If Group 249 is elected, the claim will be searched to the extent that it reads on a method of screening a compound for effectiveness in altering the expression of a polynucleotide comprising SEQ ID NO: 39, and so on. If Applicant elects one of Groups 246-280, please indicate which SEQ ID NO is to be searched.

Groups 281-315, claim 29, in part, drawn to a method of assessing the toxicity of a test compound by treating a biological sample comprising a polynucleotide comprising SEQ ID NO: 36-70, respectively. If Group 281 is elected, the claim will be searched to the extent that it reads on a biological sample comprising SEQ ID NO: 36. If Group 282 is elected, the claim will be searched to the extent that it reads on a biological sample comprising SEQ ID NO: 37. If Group 283 is elected, the claim will be searched to the extent that it reads on a biological sample comprising SEQ ID NO: 38. If Group 284 is elected, the claim will be searched to the extent that it reads on a biological sample comprising SEQ ID NO: 39, and so on. If Applicant elects one of Groups 281-315, please indicate which SEQ ID NO is to be searched.

Groups 316-350, claims 30, 33, and 35, in part, drawn to a method for a diagnostic test for a condition or disease associated with the expression of IRAP in a sample, the method comprising combining the biological sample with an antibody that binds to a polypeptide comprising SEQ ID NO: 1-35, respectively. If Group 316 is elected, the claims will be searched to the extent that they read on an antibody that binds to a polypeptide comprising SEQ ID NO: 1. If Group 317 is elected, the claims will be searched to the extent that they read on an antibody that binds to a polypeptide comprising SEQ ID NO: 2. If Group 318 is elected, the claims will be searched to the extent that they read on an antibody that binds to a polypeptide comprising SEQ ID NO: 3. If Group 319 is elected, the claims will be searched to the extent that they read on an antibody that binds to a polypeptide comprising SEQ ID NO: 4, and so on. If Applicant elects one of Groups 316-350, please indicate which SEQ ID NO is to be searched.

Groups 351-385, claims 36 and 39, in part, drawn to methods of preparing antibodies that bind to polypeptides comprising SEQ ID NOS: 1-35, respectively. If Group 351 is elected, the claims will be searched to the extent that they read on an antibody that binds to a polypeptide comprising SEQ ID NO: 1. If Group 352 is elected, the claims will be searched to the extent that they read on an antibody that binds to a polypeptide comprising SEQ ID NO: 2. If Group 353 is elected, the claims will be searched to the extent that they read on an antibody that binds to a polypeptide comprising SEQ ID NO: 3. If Group 354 is elected, the claims will be searched to the extent that they read on an antibody that binds to a polypeptide comprising SEQ ID NO: 4, and so on. If Applicant elects one of Groups 351-385, please indicate which SEQ ID NO is to be searched.

Groups 386-420, claims 44 and 45, in part, drawn to a method of detecting and/or purifying a polypeptide comprising SEQ ID NO: 1-35, respectively. If Group 386 is elected, the claims will be searched to the extent that they read on a polypeptide comprising SEQ ID NO: 1. If Group 387 is elected, the claims will be searched to the extent that they read on a polypeptide comprising SEQ ID NO: 2. If Group 388 is elected, the claims will be searched to the extent that they read on a polypeptide comprising SEQ ID NO: 3. If

Group 389 is elected, the claims will be searched to the extent that they read on a polypeptide comprising SEQ ID NO: 4, and s on. If Applicant elects one of Groups 386-420, please indicate which SEQ ID NO is to be searched.

Groups 421-455, claim 47, in part, drawn t a method of generating an expression profile containing a polynucleotide comprising SEQ ID NO: 36-70, respectively. If Group 421 is elected, the claim will be searched to the extent that it reads on a polynucleotide comprising SEQ ID NO: 36. If Group 422 is elected, the claim will be searched to the extent that it reads on a polynucleotide comprising SEQ ID NO: 37. If Group 423 is elected, the claim will be searched to the extent that it reads on a polynucleotide comprising SEQ ID NO: 38. If Group 424 is elected, the claim will be searched to the extent that it reads on a polynucleotide comprising SEQ ID NO: 39, and so on. If Applicant elects one of Groups 421-455, please indicate which SEQ ID NO is to be searched.

The inventions listed as Groups 1-325 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Claim 1 broadly encompasses the polypeptide sequences of 35 different proteins. The polypeptide sequences of Groups 1-35 are composed of different amino acids and are structurally and functionally unrelated, each to each other. The only feature linking the polypeptides is that they are immune response associated proteins. Wang et al. (NCBI Accession No. AAA61198) teach the amino acid sequence of tumor necrosis factor, which is an immune response associated protein. Thus, the technical feature of claim 1 is not a contribution over the prior art and is not considered a special technical feature. Accordingly, each of the 35 different amino acid sequences recited in claim 1 are not so linked under PCT Rule 13.1 and are thus placed in Groups numbered 1-35, respectively. Also, unity of invention is lacking for Groups 36-455, because the PCT rules do not provide for the search and examination of unrelated products or more than one method of use and one method of making for the first claimed product.

Groups 1-35 recite the technical feature of polypeptides, which is not required for the products of Groups 36-140.

Groups 36-70 recite the technical feature of polynucleotides, which is not required for the products of Groups 1-35 and 71-140.

Groups 71-105 recite the technical feature of a transgenic organism, which is not required for the products of Groups 1-70 and 106-140.

Groups 106-140 recite the technical feature of antibodies, which is not required for the products of Groups 1-105.

Groups 141-175 recite the technical feature of detecting target polynucleotides, which is not required for the methods of Groups 176-455.

Groups 176-210 recite the technical feature of treating a disease, which is not required for the methods of Groups 141-175 and 211-455.

Groups 211-245 recite the technical feature of screening for compounds that modulate the activity of a polypeptide, which is not required for the methods of Groups 141-210 and 246-455.

Groups 246-280 recite the technical feature of screening a compound for effectiveness in altering the expression of a polynucleotide, which is not required for the methods of Groups 141-245 and 281-455.

Groups 281-315 recite the technical feature of assessing the toxicity of a test compound, which is not required for the methods of Groups 141-280 and 316-455.

Groups 316-350 recite the technical feature of a diagnostic test, which is not required by the methods of Groups 141-315 and 351-455.

Groups 351-385 recite the technical feature of preparing antibodies, which is not required for the methods of Groups 141-350 and 386-455.

Groups 386-420 recite the technical feature of detecting and purifying polypeptides, which is not required for the methods of Groups 141-385 and 421-455.

Groups 421-455 recite the technical feature of generating an expression profile, which is not required for the methods of Groups 141-420.

Continuation of B. FIELDS SEARCHED Item 3:
EAST, MEDLINE, CAPLUS, SCISEARCH, BIOSIS
search terms: SEQ ID NO: 1, CD6